

and pharmaceutically adceptable salts thereof wherein

X is N or CH;

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DOZUMBE CHOYCO

is a cyclic 5-10 membered cyclic ring which

is saturated and which may contain 1 or 2 additional ring heteroatoms selected from the group consisting of 0, S and N, with the remaining ring atoms being carbon atoms;

 R_1 is $(CH_2)n - \frac{1}{2} - (R_5)$, Q, hydrogen or lower

alkyl;

 R_2 is hydrogen or Q;

Q and Q' may be the same or different and are independently

 $(CH_2) n_1 - Y - (CH_2) n_2 - CH_7$ R_4

Z is a chemical bond, CH₂, O, S or NH; Y is CH₂, O, S or NH;

 R_3 , R_4 and R_5 are independently cyclic rings containing 6-14 ring carbon atoms, and containing no hetero ring atoms, which cyclic rings may be completely saturated, partially unsaturated or aromatic, and which

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are unsubstituted or substituted with an electron donating group or electron withdrawing group;

 $$\rm R_{3}$$ and $\rm R_{4}$$ may be fused to form a cyclic ring structure containing 12-28 carbon atoms;

 R_6 , R_{10} and R_{11} are independently hydrogen or lower alkyl, which is unsubstituted or substituted with an electron withdrawing group or electron donating group;

 n_2 is 0-8; and

n and n_1 are independently 1-8, provided that either R_1 is Q or R_2 is Q'.

2. The compound according to Claim 1 wherein Y is O or CH_2 .

3. The compound according to Claim 1 wherein n_2 is 0.

 $\mbox{4.} \quad \mbox{The compound according to Claim 1 wherein} \\ \mbox{n_1 is 1 and n_2 is 0.}$

5. The compound according to Claim 1 wherein R_1 is $(CH_2)_n$ - Z - $R_5,$ hydrogen or lower alkyl and R_2 is Q'.

6. The compound according to Claim 1 wherein $\ensuremath{R_1}$ is Q and $\ensuremath{R_2}$ is Q'.

7. The compound according to Claim 5 having the formula:

R₁

8. The compound according to Claim 7 having the formula:



The compound according to Claim 7 or 8

wherein Y is 0.

The compound according to any one of 10. or 9 wherein R_3 and R_4 are independently

aromatie

The compound according to Claim 5 having 11.

the formula:

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wherein

 n_3 and n_4 are independently 1-5;

 n_1 is 1-8;

 R_1 is $(CH_2)n - Z - R_5$, hydrogen or lower alkyl,

 \boldsymbol{R}_{7} and each \boldsymbol{R}_{8} are independently hydrogen, an electron donating or electron withdrawing group;

Z is CH_2 , O, S or NH; and

 $R_{\scriptscriptstyle{5}}$ is a cyclic ring containing 6-14 ring carbon

atoms and is aromatic and may be unsubstituted or

substituted with an electron withdrawing group or

electron donating group.

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 $\ensuremath{\mathtt{R}}_9$ is hydrogen, an electron donating group or electron withdrawing group and;

 n_s is 1-5.

13. The compound according to Claim 1, 10 or 12 wherein n is 1.

14. The compound according to any one of Claims 1, 11 or 12 wherein the electron donating group is amino, hydroxy or lower alkoxy, and the electron withdrawing group is halo, lower alkyl, nitro or nitrile.

15. The compound according to Claim 14 wherein the electron donating group is lower alkoxy and the electron withdrawing group is halo.

16. The compound according to Claim 11 or 12 wherein $\ensuremath{R_{7}}$ and $\ensuremath{R_{8}}$ are halo.

17. The compound according to Claim 1 having the formula:

$$R_2$$

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$$\bigcap_{\substack{N\\\\\\\\R_1}}^{R_2} \qquad \text{or} \qquad \bigcap_{\substack{N\\\\\\\\R_1}}^{R_2}$$

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The compound according to Claim 17 or 18 19.

wherein Y is 0.

The compound according to Claim 17, 18 or wherein R_3 and R_4 are independently aromatic. 21. The compound according to Claim 17 having

the formula:

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wherein

 n_3 and n_4 are independently 1-5;

 n_1 is 1-8;

 R_1 is $(CH_2)n - Z - R_5$, hydrogen or lower alkyl; each $\ensuremath{R_{7}}$ and each $\ensuremath{R_{8}}$ are the same or different

and are independently hydrogen, an electron donating or electron withdrawing group;

Z is CH₂, O, S or NH;

 $$\rm R_{5}$$ is a cyclic ring containing 6-14 ring carbon atoms and is aromatic and may be unsubstituted or substituted with an electron withdrawing group or electron donating group.

22. The compound according to Claim 17 having the formula:

$$(CH_2)n_1 - 0$$

$$(R_7)n_4$$

$$(R_8)n_3$$

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wherein

 n_3 and n_4 are independently 1-5;

 n_1 is 1-8;

 R_1 is $(CH_2)n-Z-R_5$, hydrogen or lower alkyl; each R_7 and each R_8 are the same or different and are independently hydrogen, an electron donating or electron withdrawing group;

Z is CH_2 , O, S or NH;

 $$R_{5}$$ is a cyclic ring containing 6-14 ring carbon atoms and is aromatic and may be unsubstituted or substituted with an electron withdrawing group or electron donating group.

The compound according to Claim 22 having 23. the formula:

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wherein

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each $\ensuremath{R_{7}}$ and each $\ensuremath{R_{8}}$ are the same or different and are independently hydrogen, an electron donating or electron withdrawing group;

 $\ensuremath{R_9}$ is hydrogen, an electron donating group or electron withdrawing group;

 $\rm n_{\rm 3},\ n_{\rm 4}$ and $\rm n_{\rm 5}$ are independently 1-5; and \boldsymbol{n} and \boldsymbol{n}_1 are independently 1-8.

24. The compound according to Claim 21 having the formula:

$$(R_{1}) n_{1} - 0$$

$$(R_{2}) n_{1}$$

$$(R_{3}) n_{3}$$

$$(R_{3}) n_{5}$$

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wherein

each R_{7} and each R_{8} are the same or different and are independently hydrogen, an electron donating or electron withdrawing group;

 $\ensuremath{R_9}$ is hydrogen, an electron donating group or electron withdrawing group;

 $\rm n_3,\ n_4$ and $\rm n_5$ are independently 1-5; and $\rm n$ and $\rm n_1$ are independently 1-8.

 $\,$ 25. The compound according to any one of Claims 21-24 wherein $n_{_{\rm 1}}$ is 1.

26. The compound according to any one of Claims 21-24 wherein the electron donating group is amino, hydroxy or alkoxy and the electron withdrawing group is halo, lower alkyl, nitro or nitrile.

wherein 10

 R_1 is Q and R_2 is hydrogen or Q'.

28. The compound according to Claim 27 wherein

 R_1 is

$$(CH_2)n - (CH)$$
.

2.0

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The compound according to Claim 28 wherein 29.

n is 1.

The compound according to any one of 30.

Claims 27-29 wherein $R_{\scriptscriptstyle 3}$ and $R_{\scriptscriptstyle 4}$ are independently phenyl. The compound according to Claim 27 having

the structure

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wherein

 $\rm R_{13}$ and $\rm R_{12}$ are independently hydrogen, an electron donating group or an electron withdrawing group.

32. The compound according to Claim 31 wherein

 R_2 is H.

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33. The compound according to Claim 31 wherein \mathbf{R}_2 is

 $(CH_2) n_1 - Y - (CH_2) n_2 - CH$

wherein

Y is O, S, NH or CH₂;

 $\rm R_3$ and $\rm R_4$ are independently the same or different and are cyclic rings containing 6-14 ring carbon atoms, which cyclic rings are aromatic and which are unsubstituted or substituted with an electron donating group or an electron withdrawing group;

 n_1 is 1-8, and n_2 is 0-8.

34. The compound according to Claim 33 wherein Y is O.

- 35. The compound according to Claim 33 or 34 wherein R_3 and R_4 are independently phenyl rings which are unsubstituted or substituted with an electron donating group or electron donating groups.
- 36. The compound according to Claim 33 wherein n_1 is 1.
- 37. The compound according to Claim 33 wherein n_2 is 0.
- 38. The compound according to Claim 33 wherein $n_1 \mbox{ is } 1 \mbox{ and } n_2 \mbox{ is } 0 \mbox{.}$
- 39. The compound according to Claim 31 having the formula:

CH₂ 10 15 wherein 20

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 $\mathbf{R}_{12},~\mathbf{R}_{13},~\mathbf{R}_{14}$ and \mathbf{R}_{15} are independently hydrogen, electron withdrawing group or electron donating group.

40. A stereoisomer of the compound of Claim 1.

A pharmaceutical composition comprising a 41. cytostatic effective amount of a compound according to Claim 1 and a pharmaceutically acceptable carrier therefor.

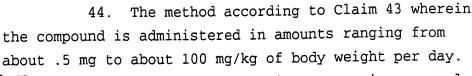
42. A method of inhibiting cancer cell proliferation in a mammal in need of such treatment comprising administering to said mammal a cytostatic effective amount of a compound according to any one of Claims 1, 7, 8, 11, 12, 17, 18, 21, 22, 23, 24 or 31.

43. The method according to Claim 42 wherein said mammal is a human.

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45 A method of treating cancer in a mammal in need thereof comprising administering to said mammal an effective amount of a compound according to any one of Claims 1, 7, 8, 11, 12, 17, 18, 21, 22, 23, 24 or 31.

46. A substantially pure compound of Claim 1.

A method of treating cancer in an animal afflicted with such disease which comprises administering to an animal in need of such treatment an organic calcium blocker that inhibits the entry of calcium ions across the cell membrane through a T-like calcium channel in cancer cells in response to a mitogenic stimulus, said calcium blocker being present in an amount effective to inhibit the passage of calcium into the cell.

- 48. The method according to Claim 47 in which the compound blocks calcium entry into the cell by interacting with the $\alpha 1$ subunit of a calcium channel.
- $49\,.$ The compound according to Claim 1 which contains 1 additional heteroatom selected from the group consisting of O and N.
- 50. The compound according to Claim 1 which contains no additional heteroatoms.
- 51. The method according to Claim 48 wherein the $\alpha 1$ subunit is an $\alpha 1 G$ or $\alpha 1 H$